IDWeek 2022 | Poster #P645

Trends in the Susceptibility of US *Acinetobacter baumannii-calcoaceticus* Species Complex and *Stenotrophomonas maltophilia* Isolates to Minocycline, 2014–2021

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Introduction

- *Acinetobacter baumannii-calcoaceticus* species complex (ACB) and *Stenotrophomonas maltophilia* (SM) are opportunistic, non-fermentative Gram-negative organisms that can cause serious hospital-acquired infections in immunocompromised patients.
- Carbapenem-resistant *Acinetobacter baumannii* is an urgent threat listed in the Antibiotic Resistance Report (CDC, 2019).
  - These pathogens are inherently resistant to several common drug classes and often acquire other resistance mechanisms, making them difficult to treat.
  - In addition, a small number of drugs have approved CLSI breakpoints for these organisms in M100, limiting the treatment options.
- In this study, we analyzed the susceptibility of contemporary ACB and SM isolates to minocycline (MIN) and levofloxacin (LEV) as well as ACB to meropenem (MER) and SM to trimethoprim-sulfamethoxazole (T/S).
- Isolates were collected as a part of the SENTRY Antimicrobial Surveillance Program from 2014–2021.

Methods

- Isolates were collected from hospitalized patients in 36 US medical centers from 9 US census regions.
  - Hospitals submitted 1 isolate per patient per infection episode that met local criteria for being the likely causative pathogen.
- Identification was performed by the submitting laboratory and confirmed by JMI Laboratories with matrix-assisted laser desorption ionization-time of flight mass spectrometry or other standard methods as required.
- Isolates were tested for susceptibility (S) to MIN, LEV, MER, and T/S using the CLSI broth microdilution method (CLSI M07, 2018).
- All infection types were included in the analysis.
- CLSI (M100, 2022) breakpoints were applied.

Results

- A total of 1,029 ACB and 1,520 SM were tested.
  - Pneumonia in hospitalized patients was the most common infection from which both ACB (57.0%) and SM (73.9%) were isolated (Figure 1).
- The %S to the agents tested for the organisms in this study are shown in Figures 2 and 3.
- MIN had the highest overall %S for ACB (86.2%S) and SM (99.5%S).
  - Overall %S to LEV was 59.3% and 77.9% for ACB and SM, respectively.
  - Overall %S to MER was 61.5% for ACB.
  - Overall, 95.4% of SM were S to T/S.
- The %S of ACB and SM varied over the 8-year period studied.
  - ACB %S to MIN decreased from 86.1% in 2019 to 80.6% in 2020 but rebounded to 86.2% in 2021 (Figure 2).
    - LEV and MER showed an overall trend of increasing %S for ACB.
    - LEV showed the largest decrease in %S in 2020 and 2021 from 67.3% to 61.5%.
  - SM had stable %S to MIN and T/S (>98.3% and >93.7%, respectively; Figure 3).
    - %S to LEV varied from a high of 84.3%S (2015) to the low of 69.2%S (2018), with %S increase to 81.5% and 82.8% in 2020 and 2021, respectively.
- The cumulative % inhibition of ACB and SM by MIN, LEV, and MER is shown in Figures 4 and 5.
  - MIN was more active than LEV or MER against ACB.
  - MIN and T/S were more active than LEV against SM.
  - MIN %S to MER-R ACB was 66.2%, LEV %S was 0.8%.
  - MIN %S to T/S-R SM was 90.0%, LEV %S was 25.7%.

Figure 1. Infection types with *A. baumannii-calcoaceticus* complex and *S. maltophilia* isolates

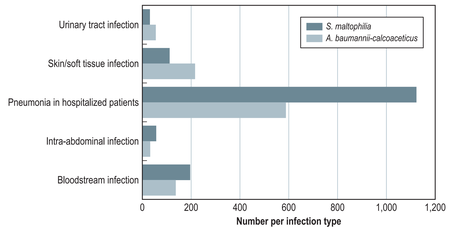
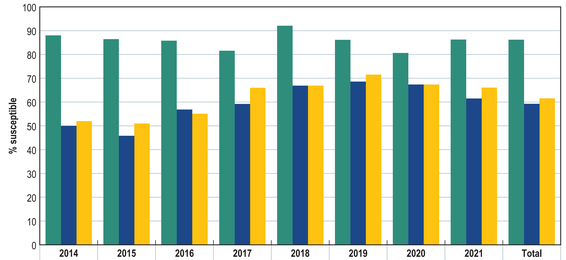
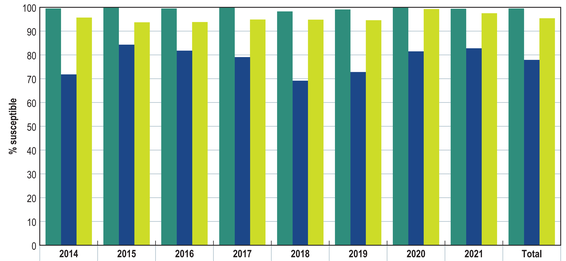


Figure 2. Percent susceptibility of *A. baumannii-calcoaceticus* species complex by year to minocycline (MIN), levofloxacin (LEV), and meropenem (MER)



	2014	2015	2016	2017	2018	2019	2020	2021	Total
MIN	88.0	86.5	85.8	81.6	92.1	86.1	80.6	86.2	86.2
LEV	50.0	45.8	56.8	59.2	66.9	68.6	67.3	61.5	59.3
MER	52.0	51.0	55.1	66.0	66.9	71.5	67.3	66.1	61.5

Figure 3. Percent susceptibility of *S. maltophilia* by year to minocycline (MIN), levofloxacin (LEV), and trimethoprim/sulfamethoxazole (T/S)



	2014	2015	2016	2017	2018	2019	2020	2021	Total
MIN	99.5	100.0	99.5	100.0	98.3	99.1	100.0	99.4	99.5
LEV	71.8	84.3	81.8	79.1	69.2	72.8	81.5	82.8	77.9
T/S	95.7	93.7	93.8	94.9	94.8	94.6	99.3	97.5	95.4

Figure 4. Cumulative percent inhibition of *A. baumannii-calcoaceticus* species complex by minocycline (MIN), levofloxacin (LEV), or meropenem (MER)

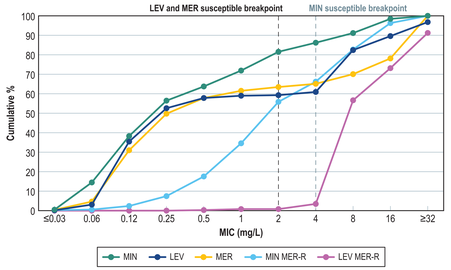
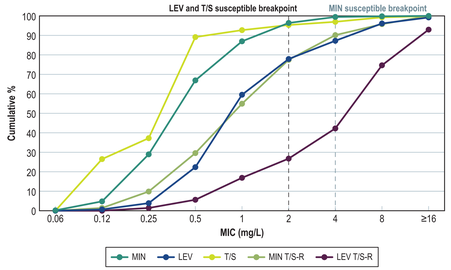


Figure 5. Cumulative percent inhibition of *S. maltophilia* by minocycline (MIN), levofloxacin (LEV), or trimethoprim/sulfamethoxazole (T/S) and MIN and LEV with T/S-R isolates



Conclusions

- %S to MIN against both ACB and SM remained stable and was higher than other agents tested.
  - Both ACB and SM have limited therapeutic alternatives.
  - ACB showed <6% decrease in %S to all 3 agents in 2020 and 2021.
  - SM showed no decrease in %S in 2020 and 2021 for the 3 agents tested.
- MIN was active against MER-R ACB and against SXT-R SM, the 2 agents that are often used as first line therapies.
- These *in vitro* data suggest that MIN remains a useful treatment option for infections caused by ACB or SM.

Funding

This study was supported by Melinta Therapeutics. Authors are employees of JMI Laboratories, which was paid consultant to Melinta Therapeutics in connection with the development of this poster.

Acknowledgments

The authors thank all participant centers for providing isolates.

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